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Case Report

Rapid Progression may Indicate Pathological Under-diagnosis in a Case of Spinal Cord Astrocytoma

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Abstract

Introduction: Most intramedullary spinal cord tumors are low-grade gliomas and are usually characterized by slow progression. This is a case of a patient histologically diagnosed as low grade intramedullary astrocytomas but with fast growing behavior.

Presentation of Case: A 67-year-old man was diagnosed with a low-grade but-fast-growing intramedullary astrocytoma. He lost his ability to walk within 1 month after symptom onset. Preoperative spinal MRI showed an intramedullary lesion from T2 to T4. Decompression surgery was performed at the T2–T4 level and the tumor was partially removed, followed by standard radiotherapy and TMZ chemotherapy. Histological examination showed a low-grade astrocytoma (WHO grade II). However, the tumor rapidly progressed and the patient eventually developed disability in all four limbs. MRI then showed the tumor to extend from C2 to T7. The patient died of respiratory failure 17 months after his surgery.

Conclusions: This case indicated that for patient with low-grade spinal cord astrocytoma, if the clinical progression does not match the pathological diagnosis, the treatment plan should be reconsidered.

Keywords: Intramedullary spinal cord tumors (IMSCTs); low grade astrocytoma; sampling error; fast growing; tumor heterogeneity

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Introduction

Intramedullary spinal cord tumors (IMSCTs) are rare; they account for only 2–4% of all central nervous system tumors [1]. The most common IMSCTs in adults are ependymomas, followed by astrocytomas. Histological grade is the most important predictor of survival in patients with intramedullary astrocytoma [2]. The World Health Organization (WHO) characterizes astrocytomas into four grades: pilocytic (grade I), diffuse or low-grade (grade II), anaplastic (grade III) and glioblastoma (GBM; grade IV). Low grade astrocytomas (grade I–II) are associated with a better prognosis than high grade (grade III–IV), with 5-year life expectancy exceeding 70% [3]. In this case, a patient with a grade II astrocytoma that arose at the thoracic cord but progressed with unusual speed to extend over 10 spinal levels by 16 months after the surgery.

The purpose of this case report is not only present a phenomenon of a patient with a low-grade but fast-growing astrocytoma, but to stress the effect of potentially misleading errors in tumor sampling.

Case presentation

A 67-year-old man presented in May 2016 with a 1-month history of back pain, progressive weakness of bilateral lower limbs and urinary dysfunction. He had no relevant family history of illness. He complained of losing the ability to walk within 30 days from the onset of symptoms. Neurological examination revealed that both lower limbs had grade 2 strength. Thoracic spine MRI showed a contrast-enhancing intramedullary lesion at T2 to T4 [Fig. 1A，B].

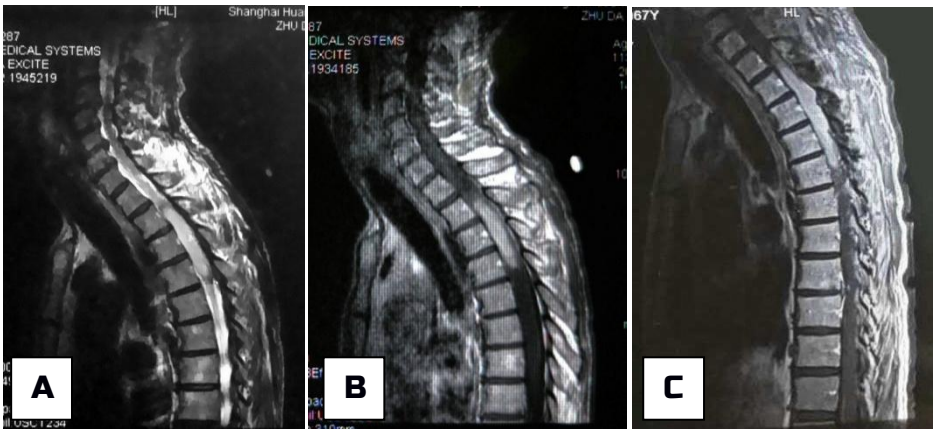

Fig.1 Preoperative T2-weighted (A) and Gd-enhanced T1-weighted (B) MR images show an intramedullary lesion at T2–T4 level. (C) Gd-enhanced T1-weighted MRI 4 months after the surgery and irradiation therapy show the lesion to have enlarged from T1 to T5.

The patient underwent a partial tumor resection at the T2–T4 level. Pathology showed that oval-nucleus tumor cells with abundant protuberances were distributed at medium density. The tumor nuclei had mild heterogeneity [Fig. 2A, B]. The tumor cells were GFAP+ [Fig. 2C]; the Ki-67 proliferative index was 4% [Fig. 2D]; and molecular pathology showed that the tumors had a methylated MGMT promoter with 1p/19q co-deletion, and wild-type *TERT* and *IDH-1/2*.

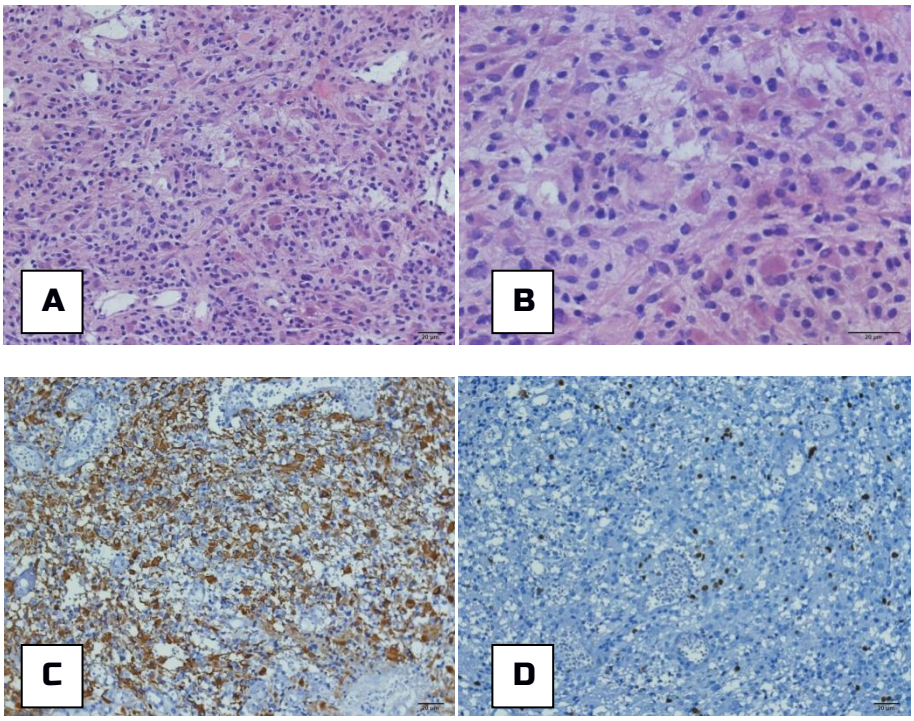

Fig.2 A (H&E, ×200) and B (H&E, ×400): Oval-nucleus tumor cells with abundant protuberances; medium-dense distribution, and mildly heterogeneous tumor nuclei.
C: Tumor cells were GFAP+. D: The Ki-67 proliferative index was 4%.

Postoperatively, the patient become completely paraplegic. Two months after the partial T2–T4 tumor resection, the patient received radiotherapy (1.8 Gy/day, 5 days a week for 5 weeks; total dosage: 45 Gy). As MGMT promoter methylation is associated with higher sensitivity to cytotoxic therapy, he also received 6 cycles of TMZ chemotherapy (1^{st} cycle: TMZ 150 mg/m^2 for Days 1–5 of a 28-day cycle; 2^{nd}–6^{th} cycles: TMZ 200 mg/m^2 for Days 1–5 of 28-day cycles).

Serial MRIs at 4 months [Fig. 1C] and 10 months [Fig. 3] after the surgery showed the tumor extending from thoracic cord to the cervical cord at C6. By April, 2017, the patient had deteriorated and developed disability in all four limbs. Cervical and thoracic MRI showed that the tumor had rapidly extended from C2 to T7 [Fig.4]. The patient died of respiratory failure 17 months after the surgery.

Fig. 3 T2-weighted (A) and Gd-enhanced T1-weighted (B) MRI 10 months after the surgery and 1 month after 6 cycles TMZ chemotherapy.

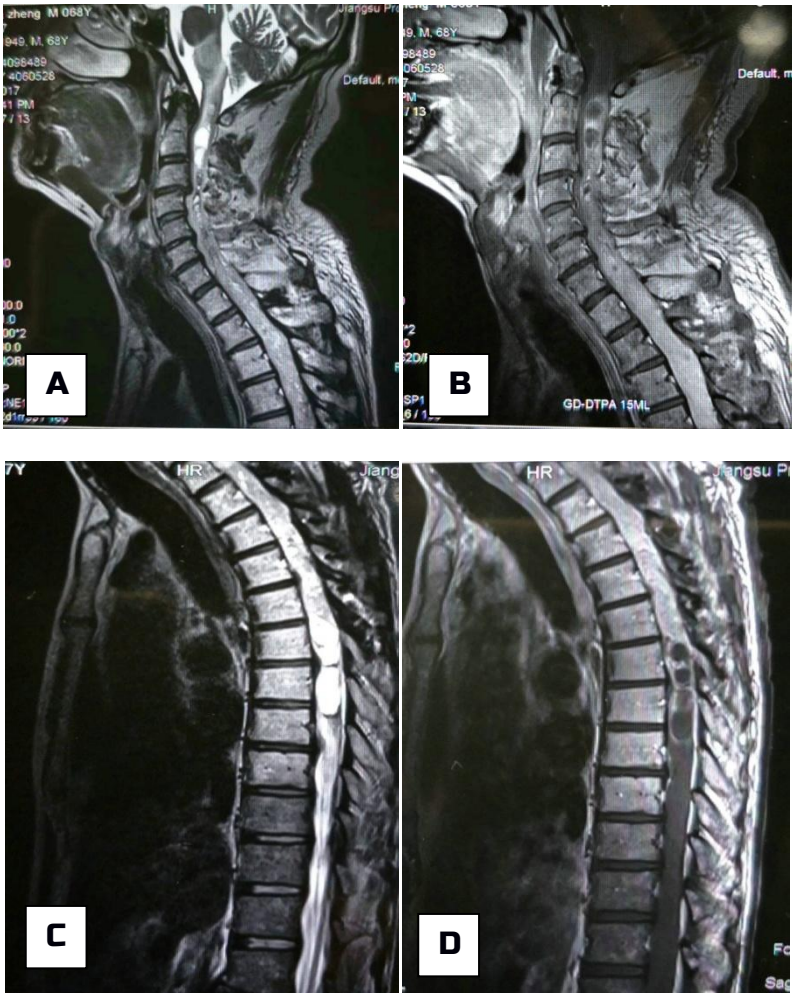

Fig. 4 T2-weighted (A, C) and Gd-enhanced T1-weighted (B, D) MRI 16 months after the surgery show the tumor to have rapidly extended, from C2 to T7.

Discussion

Reported predictors of outcome after surgery for spinal cord astrocytomas include tumor histological grade, preoperative functional status, and the extent of resection. The study of Mohamad *et al.* confirms the importance of histological grade as the most significant prognostic variable in patients with spinal cord astrocytomas [4]. Most spinal cord astrocytomas are slow-growing lesions, and patients with thoracic astrocytomas have a significantly better prognosis than those with cervical astrocytomas [5]. However, in this case, the patient had a low-grade thoracic astrocytoma with rapid progression that did not match the expected prognosis. Ryu *et al.* also observed two cases of low-grade spinal cord astrocytoma for which pathologic grade was not concordant with clinical behaviour. They considered heterogeneity of the tumors might have led to under-grading [6]. Unlike ependymomas, astrocytomas are more infiltrative and have unclear boundaries between tumor and normal spinal cord tissue. Raco *et al.* reviewed 202 patients who underwent resection of IMSCTs, and found that only 12% Grade II astrocytomas were completely removed [7]. Among patients who underwent partial removal or biopsy of their tumors, specimens tended to be very small, and might often have not accurately represented their entire tumors in pathological assessments [8]. Considering the possibility of sampling errors, low-grade astrocytomas should be closely monitored. Ito *et al.* investigated clinical factors that are useful in the diagnosis of malignant IMSCTs. In their retrospective study, the average period from onset until a patient becoming non-ambulatory was 28.9 days for high-grade (grade IV) tumor. They concluded that rapid progression of paralysis, especially walking ability, was a more valuable clinical indicator for differentiating between malignant and benign intramedullary tumors, than radiological or pathological information [9]. As our patient lost his ability to walk only 1 month after onset, and underwent partial resection of the tumor, the specimen might not have been obtained from an appropriate or representative part of the tumor.

For low-grade astrocytomas located at the thoracic spinal cord, the goal of treatment is to prevent loss of neurologic function below the level of the tumor. But for patients with rapid progression of paralysis and complete presurgical motor and sensory loss below the level of the lesion, the goal of treatment should be to preserve function up to the tumor level. Several reports describe cordectomy [10-12] or radiocordectomy [13,14] for patients with high-grade astrocytomas who already have poor neurologic function at the thoracic or lumber spinal cord level, to prevent tumors from expanding to the cervical level. The patient in this case was initially diagnosed with a low-grade astrocytoma and underwent partial resection, radiotherapy and chemotherapy, but the tumor continued to grow, finally extending to the upper cervical cord over 16 months. A more aggressive treatment might have been executed, notwithstanding the pathological diagnosis of low-grade astrocytoma.

Conclusion

This is an unusual case of histological low grade astrocytoma but with fast growing rate. These tumors are heterogeneous; if the clinical progression does not match the pathological diagnosis, sampling

error should be considered. To avoid sampling errors, more tumor tissue or multiple samples should be collected by the surgeon, and thoroughly examined by the pathologist. If tumor progression (either pre- or post-surgical) suggests that the tumor belongs to a higher grade, more aggressive treatment should be taken.

Consent

Because the patient was died, the consent was taken from the relatives of the patient for publication of this case report.

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